

**REMARKS****Rejection of claims 11-17, 22, 24, 25, 26, 27, 30 and 31 under 35 USC § 102**

The claims were rejected as anticipated by Zaides *et al.* (Journal of General Virology, 1994) as evidenced by Rabenstein *et al.* (Biochemistry, 1995). Zaides *et al.* describe a truncated version of gp160 generated in chronically infected cells as a result of a premature stop codon in the *env* gene. This truncation deletes the cytoplasmic and transmembrane domains. The rejection relies, first, on the indication from Rabenstein *et al.* that the leucine zipper-like heptad repeat of gp160 is important for structure formation and that gp160 forms trimers in solution, and second, on the fact that naturally occurring gp160 trimers are known to not contain inter-chain disulfide linkages. The Office Action, therefore, concludes that since the gp160 of Zaides *et al.* still contains that leucine zipper-like heptad repeat and is capable of forming oligomers, Zaides *et al.* anticipates the claims. The applicants respectfully disagree.

Rabenstein *et al.* indeed state that gp160 oligomers are present as a mixture of both trimers and tetramers in solution. However, while Zaides *et al.* show that the truncated version of gp160 can form hetero-oligomers with full-length gp160, the authors never show trimer formation of gp160 or truncated forms thereof, as recited by the present claims. Furthermore, the entire *env* gene from these chronically infected cells was not sequenced, therefore it cannot be said with any degree of certainty that additional mutations were not present that would have altered the oligomerization of the truncated form of gp160. Thus, Zaides *et al.* cannot anticipate the present claims.

Nonetheless, the independent claims 13 and 22 have been amended to recite a "purified recombinant trimer," thereby obviating the instant rejection. Independent claim 11 has previously been amended to recite a "purified recombinant trimer." In light of these amendments, the applicants request that the § 102 rejections be withdrawn.

**Rejection of claims 22-31 under 35 USC § 112, first paragraph**

The claims were rejected under 35 USC § 112, first paragraph for lacking enablement. The Office Action alleged that the specification did not enable one of ordinary skill in the art to practice the invention with respect to purified recombinant trimers of HIV comprising a gp41 fragment essential for trimer formation because "neither the specification nor the art discloses the essential region in

the gp41 structure that are necessary/essential for trimer formation." For the following reasons, the applicant respectfully traverses.

As taught on p. 9, ll. 27-28, it is known that the gp41 portion of the trimer is sufficient for trimer formation. Furthermore, it is known by those skilled in the art that the gp41 hydrophobic helix is important for trimer formation. Chan and Kim, *Cell*, Vol. 93, 681-684, May 29, 1998 (copy previously provided). In fact, the article Examiner cites in the 35 USC § 102 rejection, Rabenstein *et al.*, indicates that the region of gp41 important for trimerization is known. Thus, it is well recognized not only that less than the entire gp41 protein is required for trimer formation, but exactly which portion of gp41 is required. Indeed, Example 2 of the specification describes an embodiment comprising the first 129 amino acids of the gp41 N-terminal domain, which fragment lacks the transmembrane domain, as described on p. 19. Although protein chemistry indeed is an unpredictable area of biochemistry, when the functional region of a protein has already been identified, as is the case for the structure necessary/essential for trimer formation in gp41, protein chemistry becomes far less unpredictable. Accordingly, it would be a routine matter for one skilled in the art to make and use the claimed trimer comprising a gp41 fragment essential for trimer formation. The applicants therefore respectfully submit that the claims are enabled and request that these rejections be withdrawn.

Claims 22-31 were also rejected for failing to meet the written description requirement. The Office Action alleged that the written description requirement is only met for purified gp160 trimers of HIV in which either the entire gp41 or the transmembrane deletion form of gp41 is present. The applicants respectfully traverse.

The Office Action concludes that the written description requirement is not met by looking to the standard set out for nucleic acids in *The Regents of the University of California v. Eli Lilly*, 43 USPQ2d 1398 (Fed. Cir. 1997). The court held that the written description requirement for a claim to a genus of nucleic acids is not met by a generic statement which defines the genus by their functional activity. However, the court went on to instruct how the written description could be met for such a genus claim. "A description of a genus ... may be achieved by means of a recitation of ... structural features common to the members of the genus, which features constitute a substantial portion of the genus." *Id.* at 1406.

The specification provides that the gp160 claimed in the invention can be composed of all or part of the gp41 protein (see, for example, page 7, lines 36-38). The specification goes on to describe that the claimed invention encompasses a gp160 comprising a variant in which one or more portions of gp41 is removed, provided that the gp41 portion contains the sequences necessary for trimer formation (see, for example, page 9, lines 20-30). To further describe the public how to make and use the claimed invention, the specification provides Example 2 which describes an embodiment of gp160 comprising a truncated form of gp41 that nonetheless retains the sequences necessary for trimer formation (page 19, line 1-31). As discussed above, the region of gp41 important for trimer formation is well known in the art. The applicants respectfully submit that by reciting a structural feature common to the members of the genus of compositions claimed (i.e., the sequences of gp41 necessary for trimer formation) the specification allows one skilled in the art to "visualize or recognize the identity of the members of the genus." *Id.* Therefore the skilled artisan will appreciate that the applicants had possession of claimed invention. Accordingly, the applicants request that the written description rejections be withdrawn.

#### Claim Objections

Claims 14-17 were objected to as being dependent on a rejected claim, claim 13. The applicants submit that the amendment to claim 13 has obviated the objection and therefore respectfully request that these objections be withdrawn.

#### CONCLUSION

In view of the foregoing, the Applicants respectfully request reconsideration and withdrawal of the rejections and objections. If there are any questions or comments regarding this Response or application, the Examiner is encouraged to contact the undersigned attorney as indicated below.

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